# Chemical Screening in the U.S.: A Brief Overview and Examination of the EPI Suite™ Tool

**Michael Murray, Ph.D.**
**National Wildlife Federation**

**Binational Toxics Strategy**
**Integration Workgroup**

**Chicago, IL**
**September 19, 2006**

# Introduction/Disclaimer

- Work of U.S. Environmental Protection Agency (EPA) Science Advisory Board (SAB) Estimation Programs Interface Suite™ Review Panel is not yet complete
- While a member of the Panel, this presentation reflects my views only; no endorsement by other Panel members, the Science Advisory Board, or U.S. EPA is implied
- Report of the Panel will become final when it has been approved by the Panel and the chartered Science Advisory Board

# U.S. Toxic Substances Control Act (TSCA) - 1976

- Addresses chemicals manufactured, imported, used, processed, distributed into commerce, or disposed of in U.S.
- Excludes certain substances, such as pesticides (regulated under Federal Insecticide, Fungicide, and Rodenticide Act) and food and food additives, drugs, cosmetics, etc. regulated under the Federal Food, Drug and Cosmetic Act
- Primary administrative responsibility with EPA Office of Pollution Prevention and Toxics (also administers Pollution Prevention Act of 1990)

# Major Sections of TSCA Pertaining to Chemical Data Collection and Control

| Section | Purpose |
|---|---|
| 4 | Chemical testing |
| 5 | New chemical review and control; Significant new use rules |
| 6 | Chemical regulation |
| 8 | Industry reporting of chemical data |
| 9 | TSCA's relationship to other laws |
| 14 | Disclosure of chemical data |

Source: U.S. GAO, 2005, Chemical Regulation, GAO-05-458.

# TSCA and Chemicals Assessment

- TSCA authorizes EPA to assess:
  - Existing chemicals (62,000 in commerce when EPA began reviewing chemicals in 1979)
  - New chemicals (approximately 20,000 new chemicals added to inventory after manufacturing began, of approx. 40,000 new chemical submissions)
- EPA has developed programs to test chemicals and to assess and manage potential risks from new and existing chemicals

Source: GAO, 2005.

# TSCA - Testing Policy

- TSCA authorizes EPA to require that chemical companies develop test data only under certain conditions found by agency:
  - Chemical presents unreasonable risk of injury to health or the environment
  - Is or will be produced in substantial quantities, and may have either substantial human exposure or substantial release to the environment
- EPA has used authority to require testing for fewer than 200 of original 62,000 chemicals in original inventory
- However, voluntary testing programs have been established, including High Production Volume Challenge Program (2,800 chemicals produced or imported at > 1 million lbs./year)

Source: GAO, 2005.

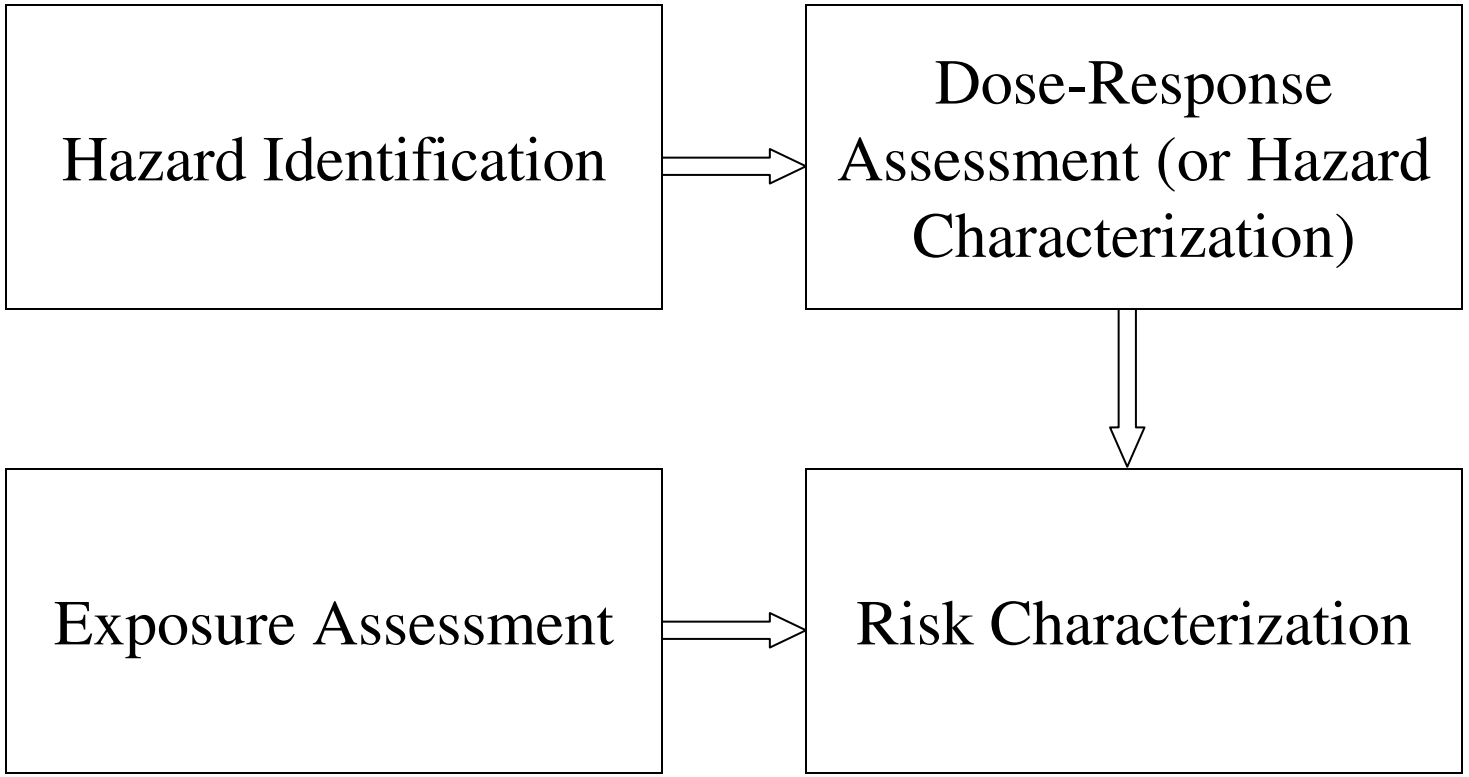
# TSCA – New Chemicals Policy

- For new chemicals, TSCA generally requires company to notify EPA at least 90 days before manufacturing, via premanufacture notice (PMN)
- While EPA has authority to promulgate rules requiring testing if certain conditions are met, TSCA does not require industry to test new chemicals for toxicity or assess other parameters (e.g. potential exposures)
- Companies generally do not voluntarily perform such testing; < 10 % of PMNs provide data on parameters such as LD50 ("An alarmingly small number of PMNs have enough publicly available data to perform a rudimentary assessment of risk."*)
- EPA has formally regulated five chemicals/classes under Section 6; but action has been taken to reduce risks of over 3,500 of 32,000 new chemicals that companies have submitted for review

Source: GAO, 2005;

*: U.S. EPA, 2005, Pollution Prevention (P2) Framework, June 2005

# Risk Assessment Paradigm




Source: U.S. National Research Council, 1993, Risk Assessment in the Federal Government: Managing the Process

# Decision-Making on New Chemicals

- Approximately 2,000 PMNs submitted by industry to EPA annually
- Factors such as yield, performance and cost are important in commercialization decisions, including consideration of alternative chemicals/processes
- Industry would typically have made many decisions early in R&D process, and many P2 opportunities would have been lost by time a PMN goes forward
- Given statutory limits and absence of hazard/risk data, EPA OPPT has relied on screening methods (in particular models based on structure-activity relationships), in conjunction with other information to assist with decision-making

Source: EPA, 2005.

# EPA Pollution Prevention (P2) Framework and Screening-Level Methods

- Most estimation methods involve hazard identification and exposure assessment steps
- Methods intended to be used either when no data are available or to supplement available data, as a screening level assessment (i.e., augmented with additional available information or call for more data)
- While EPA uses models to screen new chemical submissions, EPA is also partnering with industry to encourage companies to use the framework earlier in the product development process

Source: EPA, 2005.

# EPA Screening-Level Tools

- Chemical Screening Tool For Exposures & Environmental Releases (CHEMSTEER): Estimates occupation inhalation and dermal exposures during ind./comm. manufacturing, processing, and use of chemical, and releases associated with uses
- Exposure and Fate Assessment Screening Tool (E-FAST) Version 2.0: Provides estimate of chemical release to air, surface water and landfills from consumer products
- Estimation Programs Interface (EPI) Suite™: estimates selected physical-chemical properties and fate and transport parameters
- Other tools include ReachScan and PIRAT for pesticides

Source: EPA, Screening Level Tools Web site

# EPA P2 Framework Model Areas

Physical/chemical Properties, e.g.
- Melting point
- Vapor pressure
- Aqueous solubility

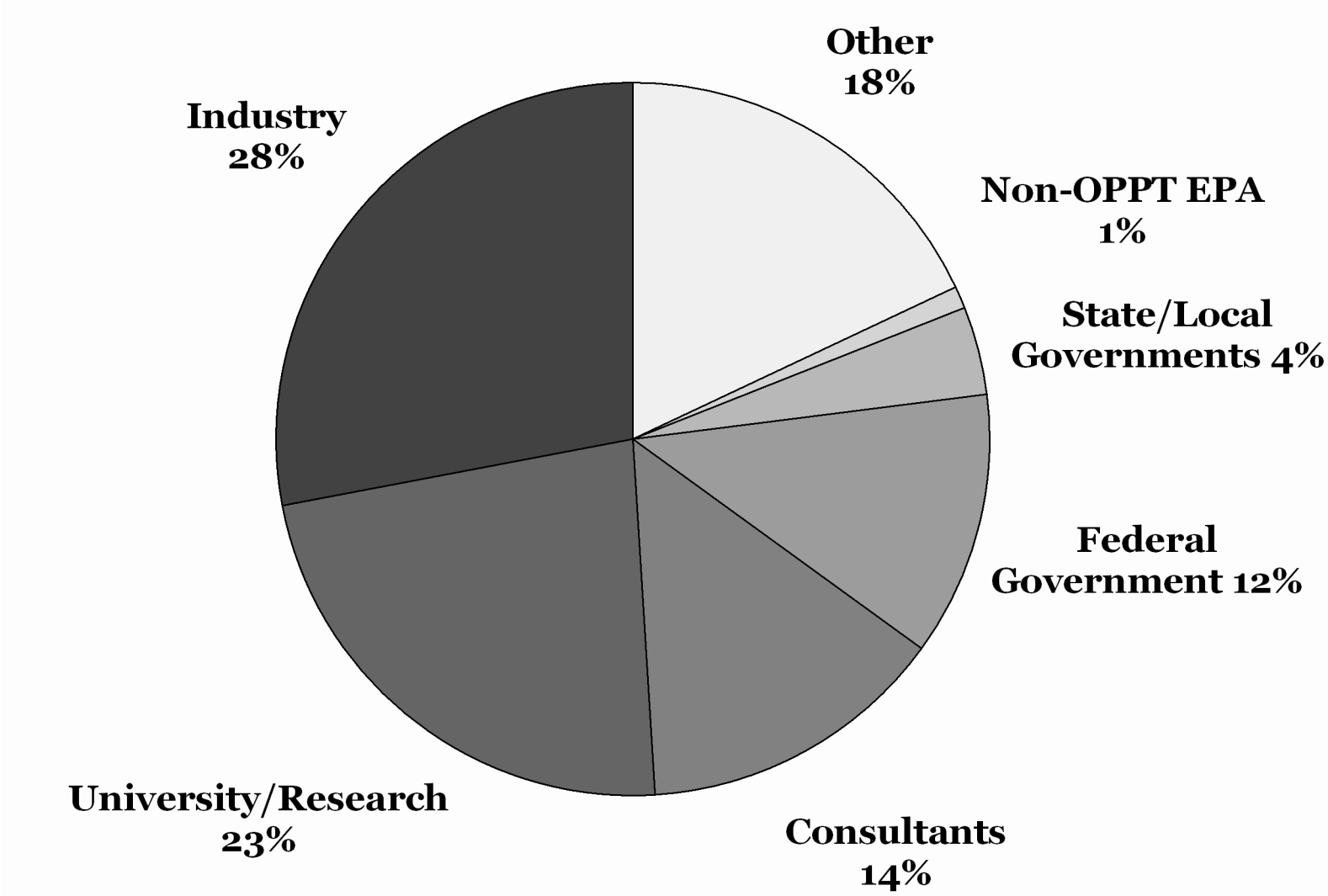
Hazards to Humans and Environment, e.g.
- Carcinogenicity potential
- Non-cancer human health effects
- Aquatic toxicity

Environmental Fate, e.g.
- Biodegradation
- Bioconcentration/bioaccumulation
- Removal in wastewater treatment plant

Exposure and/or Risk, e.g.
- Dermal exposure
- Inhalation exposure
- Exposures via surface water
- Workplace exposures

Adapted from EPA, 2005.

# Users of EPA Exposure Models




Source: EPA data from Patel, N. and Boethling, B., presentation to EPI Suite Review Panel, Feb. 22, 2006

# Estimation Programs Interface (EPI) Suite™ - Overview

- EPI Suite™ is a screening level tool consisting of models that estimate values for physical/chemical properties and selected fate and transport parameters
- Only input is chemical structure, with several options for entering chemical information
- Includes PHYSPROP file, linked to a database of measured P/C properties and fate parameters for > 40,000 chemicals
- Considered mainly for use only in absence of measured data (but measured data where available is provided via output, and via PHYSPROP database)
- Developed by Syracuse Research Corporation and EPA; now owned solely by EPA and publicly available for download from EPA OPPT Web site

# EPI Suite™ – Overview 2

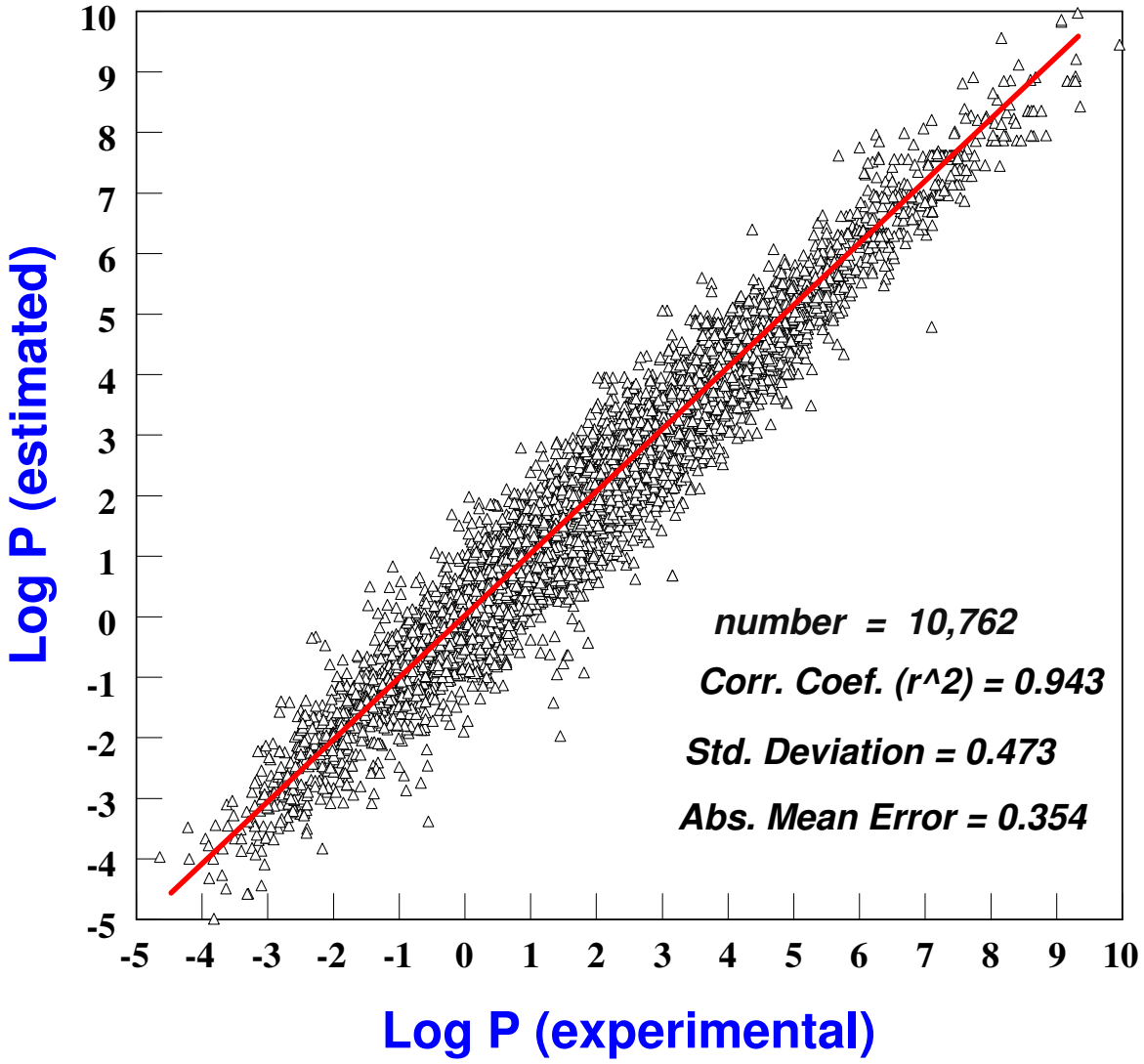
- Models for physical/chemical properties are typically based on structure-property (or structure-activity) relationships, i.e., the predictable variation in a parameter with other measured parameters or molecular descriptors
- In some cases, estimates for a parameter in EPI Suite™ derive directly from other measured or estimated parameters (e.g., WSKOW estimates aqueous solubility from the compound's Kow)
- Three environmental fate models are modifications of other models from the literature
- P/C models can be run stand-alone, in some cases with more features; the three fate/transport models cannot be run stand-alone

# Chemical Property and Fate Programs in EPI Suite™

| Name | Parameter Estimated |
|---|---|
| AOPWIN | Atmospheric oxidation |
| BCFWIN | Bioconcentration factor (BCF) |
| BIOWIN | Biodegradability |
| HENRYWIN | Henry's law constant |
| HYDROWIN | Aqueous hydrolysis |
| KOWWIN | Octanol-water partition coefficient |
| MPBPVP | Melting point, boiling point, vapor pressure |
| PCKOC | Soil sorption coefficient (Koc) |
| WSKOW | Aqueous solubility from Kow |
| WATERNT | Aqueous solubility from fragments |
| STPWIN | Removal in sewage treatment plant |
| LEVEL III | Transport/distribution via fugacity |
| WVOLWIN | Volatilization from water |

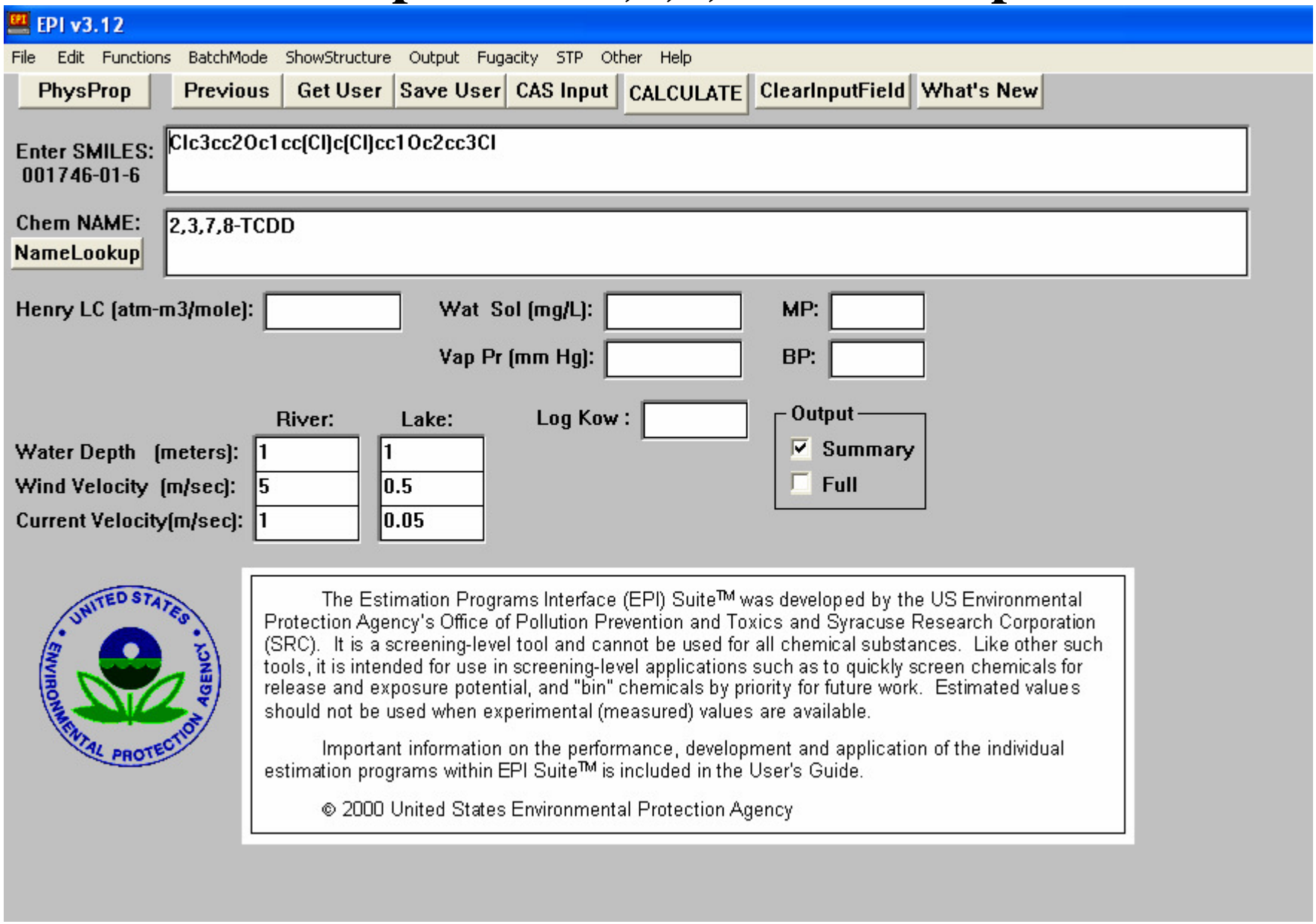
Source: Patel and Boethling, 2006; note: EPI Suite™ also contains ECOSAR aquatic toxicity model and Dermwin dermal exposure model

# Validation Data Set for KOWWIN

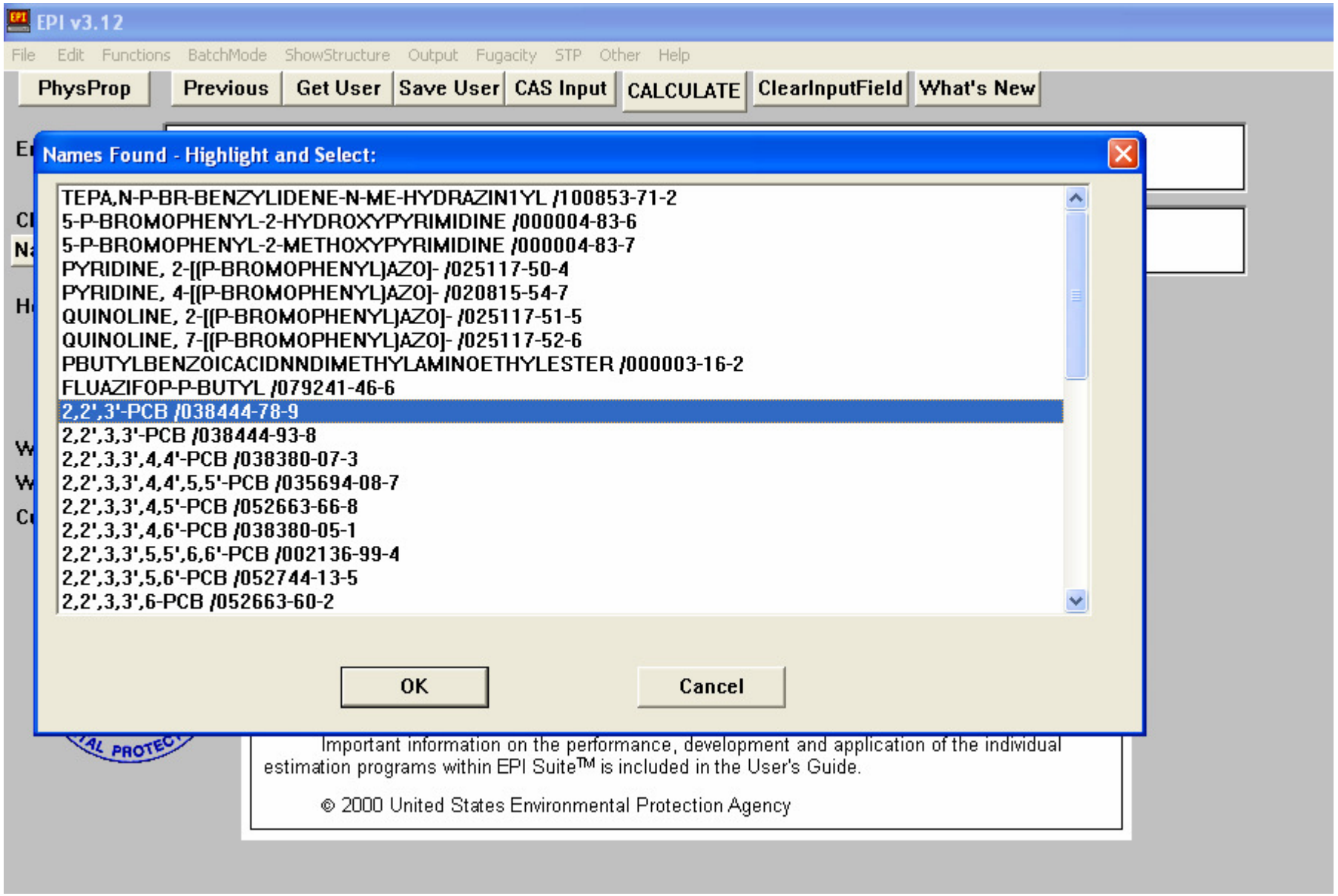



Source: Patel and Boethling, 2006

# EPI Suite™ Main Screen
# Example with 2,3,7,8-TCDD Input



# EPI Suite™ – Names Lookup (Example for PCB)



# EPI Suite™ Results – Example for 2,3,7,8-TCDD

EPI Results

Print EPA_upload Save Results Copy Help

```
SMILES : CLc3cc2Oc1cc(CL)c(CL)cc1Oc2cc3CL
CHEM   : 2,3,7,8-TCDD
CAS NUM: 001746-01-6
MOL FOR: C12 H4 CL4 O2
MOL WT : 321.98
---------------------------- EPI SUMMARY (v3.12) --------------------------
 Physical Property Inputs:
    Water Solubility (mg/L):   ------
    Vapor Pressure (mm Hg) :   ------
    Henry LC (atm-m3/mole) :   ------
    Log Kow (octanol-water):   ------
    Boiling Point (deg C)  :   ------
    Melting Point (deg C)  :   ------

 Log Octanol-Water Partition Coef (SRC):
    Log Kow (KOWWIN v1.67 estimate) =  6.92
    Log Kow (Exper. database match) =  6.80
       Exper. Ref:  Shiu,WY et al. (1988)

 Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.41):
    Boiling Pt (deg C):  379.17  (Adapted Stein & Brown method)
    Melting Pt (deg C):  141.85  (Mean or Weighted MP)
    VP(mm Hg,25 deg C):  1.95E-008  (Modified Grain method)
    MP  (exp database):  305 deg C
    VP  (exp database):  1.50E-09 mm Hg at 25 deg C

 Water Solubility Estimate from Log Kow (WSKOW v1.41):
    Water Solubility at 25 deg C (mg/L):  0.001103
       log Kow used: 6.80 (expkow database)
       no-melting pt equation used
     Water Sol (Exper. database match) =  0.0002 mg/L (25 deg C)
        Exper. Ref:  SHIU,WY ET AL. (1988)

 Water Sol Estimate from Fragments:
    Wat Sol (v1.01 est) =  0.0037973 mg/L
    Wat Sol (Exper. database match) =  0.00
       Exper. Ref:  SHIU,WY ET AL. (1988)

 ECOSAR Class Program (ECOSAR v0.99h):
    Class(es) found:
       Neutral Organics

 Henrys Law Constant (25 deg C) [HENRYWIN v3.10]:
   Bond Method :   3.53E-006  atm-m3/mole
```

# EPI Suite™ Results (2) – Example for 2,3,7,8-TCDD

EPI Results

Print EPA_upload Save Results Copy Help

```
Probability of Rapid Biodegradation (BIOWIN v4.02):
  Biowin1 (Linear Model)         :   0.1284
  Biowin2 (Non-Linear Model)     :   0.0059
Expert Survey Biodegradation Results:
  Biowin3 (Ultimate Survey Model):   1.5450  (recalcitrant)
  Biowin4 (Primary Survey Model) :   2.8761  (weeks       )
Readily Biodegradable Probability (MITI Model):
  Biowin5 (MITI Linear Model)    :   0.2023
  Biowin6 (MITI Non-Linear Model):   0.0108
Ready Biodegradability Prediction:   NO

Atmospheric Oxidation (25 deg C) [AopWin v1.91]:
  Hydroxyl Radicals Reaction:
     OVERALL OH Rate Constant =   0.7530 E-12 cm3/molecule-sec
     Half-Life =    14.204 Days (12-hr day; 1.5E6 OH/cm3)
  Ozone Reaction:
     No Ozone Reaction Estimation

Soil Adsorption Coefficient (PCKOCWIN v1.66):
     Koc    :  1.463E+005
     Log Koc:  5.165

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v1.67]:
   Rate constants can NOT be estimated for this structure!

BCF Estimate from Log Kow (BCFWIN v2.15):
   Log BCF =  4.536  (BCF = 3.436e+004)
      log Kow used: 6.80 (expkow database)

Volatilization from Water:
   Henry LC:  5E-005 atm-m3/mole  (Henry experimental database)
   Half-Life from Model River:      36.76  hours   (1.532 days)
   Half-Life from Model Lake :      399.7  hours   (16.65 days)

Removal In Wastewater Treatment:
   Total removal:              93.73  percent
   Total biodegradation:        0.78  percent
   Total sludge adsorption:    92.95  percent
   Total to Air:                0.01  percent
     (using 10000 hr Bio P,A,S)

Level III Fugacity Model:
           Mass Amount    Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
  Air       0.0748          341          1000
  Water     0.745           4.32e+003    1000
  Soil      51.1            8.64e+003    1000
  Sediment  48.1            3.89e+004    0
    Persistence Time: 1.3e+004 hr
```

# EPA Science Advisory Board EPI Suite™ Review Panel

- OPPT requested SAB review EPI Suite™
- SAB assembled a panel in early 2006 of 14 scientists with expertise in environmental chemistry/chemical property estimation techniques, chaired by Dr. Michael McFarland
- Charge to the Panel was to review the supporting science, functionality and appropriate use of the tool
- Process has included conference calls, email correspondence, and 3-day meeting in March 2006
- Panel report should be finalized this fall

# EPI Suite™ – Broader Chemicals Policy Context

- Could potentially aid in prioritizing chemicals for attention in the BTS process
- EPI Suite™ and similar programs can potentially be helpful in developing greener chemicals/processes, including through domestic programs, such as:
  - Green Chemistry Program
  - Design for the Environment
  - Sustainable Futures
- Significant chemicals policy initiatives underway internationally will also rely to varying degrees on chemical screening (e.g., updating of Canadian Environmental Protection Act Substance Lists; Registration, Evaluation and Authorisation of Chemicals (Europe); Strategic Approach to International Chemicals Management)

# Resources

U.S. EPA, Office of Pollution Prevention and Toxics
http://www.epa.gov/opptintr/index.html

Estimation Programs Interface (EPI) Suite™
http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

Syracuse Research Corporation, Databases
http://www.syrres.com/esc/databases.htm

U.S. EPA Science Advisory Board Estimation Programs Interface Suite™ Review Panel:
http://www.epa.gov/sab/panels/epi_suite_review_panel.htm

U.S. Government Accountability Office, 2005, Chemical Regulation: Options Exist to Improve EPA's Ability to Assess Health Risk and Manage Its Chemical Review Program, GAO-05-458, June 2005.

U.S. EPA, Pollution Prevention (P2) Framework, EPA-748-B-04-001, June 2005.